

the

Record

U. S. DEPARTMENT OF
HEALTH, EDUCATION, AND WELFAREVolume XIII, No. 2
January 31, 1961PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH**Aging Conference
Offers Proposals
For Wide Action**

By Mildred Sargent

Delegates from all 50 of the States and three U. S. Territories concluded their discussions at the recent 4-day White House Conference on Aging with policy statements and recommendations to help the Nation's senior citizens realize their highest potential.

Watt, Grant Praised

Dr. James Watt, Director of the National Heart Institute, who has served during the past year as Special Assistant to the Secretary for Aging, and Robert H. Grant, Executive Officer of NHI, who was Director of the Special Staff on Aging, received high praise for their work from the outgoing DHEW Secretary, Arthur S. Flemming.

Within the next 90 days, an official report of the Conference will be submitted to President Kennedy and HEW Secretary Ribicoff.

It is expected that the Conference recommendations will be widely used as a guide to actions by States, communities, the Federal Government, private organizations, and older people themselves.

Eisenhower Speaks

At the opening session in Constitution Hall, President Eisenhower delivered his last address to a Washington conference. He urged the delegates to consider "every conceivable view" of medical care.

After major discussions of this area, the Conference group concerned recommended: "It is an appropriate and desirable responsibility of the Federal Government to finance health care benefits for the aged through a contributory system of social insurance (OASDI)."

The research sections, among other recommendations, urged

(See CONFERENCE, Page 7)

**Dr. Kety to Be Head
Of Psychiatry Dept.
At Johns Hopkins**

Dr. Seymour S. Kety, Chief of the Laboratory of Clinical Science, NIMH, since 1957, has accepted appointment as Head of the Department of Psychiatry at the Johns Hopkins University School of Medicine and its hospital.

**Dr. Kety**

The appointment was announced January 15 by Milton S. Eisenhower, President of Johns Hopkins University, and Dr. Russell A. Nelson, Director of Johns Hopkins Hospital.

Dr. Kety will leave NIH for his new post in the spring.

Widely known for his work in the biology of schizophrenia, Dr. Kety recently published a review of current theories in this area. He has also been a leader in the new research field of psychopharmacology.

Upon coming to NIH in 1951, Dr. Kety served as Associate Director in Charge of Research for NINDB and NIMH.

In this position he established, organized, and supervised the combined basic science research program of these two Institutes. Concurrently, he pursued his own in-

(See DR. KETY, Page 2)

**Dr. Terry, Assistant Director of NHI,
Appointed PHS Surgeon General;
Three Other HEW Posts Filled**

In the appointment of Dr. Luther L. Terry, 49, Assistant Director of the National Heart Institute, as Surgeon General of the Public Health Service, President Kennedy chose a veteran PHS career man who has been an NIH staff member for the past 10 years.

Dr. Terry succeeds Dr. Leroy E. Burney who had served in that capacity since August of 1956.

Announcement of Dr. Terry's appointment to the top PHS post was made by the incoming President on January 15, five days prior to his inauguration.

**Dr. Terry**

At the same time Mr. Kennedy made known his selections for three other high-level positions

within the Department of Health, Education, and Welfare. They were:

Former Rep. James M. Quigley, 42, of Camp Hill, Pa., as Assistant Secretary for Federal and State Matters; Dr. Wilbur Cohen, 47, Professor of Public Welfare Administration at the University of Michigan, as Assistant Secretary for Legislative Matters; and Alan W. Willcox, 59, of Washington, D.C., General Counsel of the American Hospital Association, as General Counsel.

Becomes Acting Director

Dr. Terry was named Assistant Director of the Heart Institute in August 1958, and since December of 1959 had also served as Acting Director during the part-time absence of the Director, Dr. James Watt, designated Special Assistant to the Secretary for Aging, to assist in gerontological matters and in connection with the 1961 White House Conference on Aging.

Dr. Terry first became associated with the Public Health Service in 1942 when he was granted military leave from the University of Texas, where he was Associate Pro-

(See APPOINTMENTS, Page 8)

**Terry Brings to Job
Wide Experience in
Research, Teaching**

By Bill Sanders

Dr. Luther L. Terry brings extensive teaching, research, and clinical experience to his new post as Surgeon General of the Public Health Service.

This includes seven years as Chief of the General Medicine and Experimental Therapeutics Branch of the National Heart Institute beginning in 1951, and a continuing active interest in research work.

As Chief of GMET, Dr. Terry directed research teams engaged in such diversified projects as:

Studies to clarify the processes of amine metabolism, their alteration with disease, and their therapeutic modification by drugs;

Development of simpler, safer, more reliable means for the diagnostic evaluation of inborn heart

(See DR. TERRY, Page 8)

**'Annie,' Postponed by Thursday's Snow,
Stages Sunday Matinee Performance**

Picture on Page 8

"Annie Get Your Gun" got her powder wet Thursday night in the blizzard, but went off with a bang instead at a Sunday matinee in what might well be a precedent-setting performance.

By curtain time on Thursday, fully half of the cast and orchestra were still stranded somewhere in the city or suburbs.

However, a hardy 80 or so turned up in the audience, and those of the cast who battled it through showed their appreciation

by singing some of the show songs for them.

The CC reception desk passed the word to all inquirers that the Thursday performance would be postponed until Sunday afternoon.

By Sunday matinee time, not only those holding Thursday's tickets showed up, but a number of others—mainly children.

A further Hamster precedent was set on the night of January 17, when a special performance of "Annie" was given for CC patients, their relatives and friends.

the Record

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PERSONNEL TO PERSON

THIS MONTH marks the first anniversary of this column as a regular feature in the *NIH Record*.

During the past year, it has been the intention of the Personnel Branch to present information which is timely and of interest to NIH employees.

To insure that future coverage aligns with employee interest, PMB would appreciate receiving any suggestions that you may have concerning this column.

Employees are encouraged to informally jot down their ideas and forward them to the Program Evaluation and Reports Section, Bldg. 1, Rm. 3. Suggestions need not be signed.

SECRETARIAL TRAINING

The Employee Development Section will offer courses in Shorthand and Business English, beginning February 20.

Two shorthand classes of 30 minutes each will be held daily—one for dictation at 60-80 words per minute, the other at 80-100. Applicants must pass a qualifying exam.

The Business English class will meet Mondays, Wednesdays and Fridays—one-hour sessions—from February 20 through March 29.

Employees must be nominated by their Institutes or Divisions in order to be considered for enrollment. Classes will be filled in the order in which nominations are received.

Interested persons may obtain additional information from their administrative offices.

EXAM ANNOUNCEMENT

The Board of U. S. Civil Service Examiners at NIH announced the opening on January 11 of a new examination for Fixed Industrial Equipment Operators. The grades

Red Cross Bloodmobile To Be at NIH Feb. 14

A Red Cross Bloodmobile unit will be in Wilson Hall Tuesday, February 14, from 9 a.m. to 12:45 p.m., to receive blood donations from NIH employees.

Stressing the urgency of maintaining an adequate blood bank, Dr. Shannon in a memo to all employees said:

"Just recently one of our employees and the wife of one of our employees were in need of blood transfusions, and the American Red Cross Blood Bank's supply was so depleted that their needs went unmet.

"Whole blood," Dr. Shannon added, "is still the number one life saver of modern medicine. Give today while you are a potential donor—tomorrow you and yours may be potential recipients of this healing fluid."

range for Helper through Foreman with salaries of \$2.10 to \$4.04 per hour.

These positions are located at the NIH and several other Federal establishments within Montgomery County.

This announcement (No. B-30-1) covers the positions of Operating Engineer, Boiler Fireman, and Water Tender.

In addition to the General Option, Steam Generation, Refrigeration and Air Conditioning, and Water Supply and Testing Options are included. The Board previously announced the closing of the old examination covering these positions.

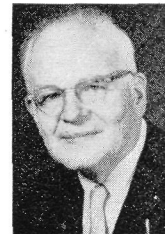
Persons interested in filing for the new exam should obtain a copy of the Exam Announcement from the Board of Examiners, Bldg. 15K, or the Recruitment and Placement Section Bldg. 1, Rm. 21.

Norway Is Free of Rabies

Norway has not had a single case of rabies in either man or animals since 1809.

Dr. John T. Edsall, NIH Guest Lecturer, Discusses Protein Molecule Structure

Dr. John T. Edsall, Professor of Biological Chemistry at Harvard University and Editor of the *Journal of Biological Chemistry*, was the guest lecturer here on January 25, in the NIH Lecture Series.



Dr. Edsall

A leading scientist in the field of physical chemistry of amino acids, Dr. Edsall spoke on "Inquiries Concerning the Fine Structure of Protein Molecules."

The discussion, concerning the status of proteins in the hierarchy of chemical molecules and biologically functional units, covered a limited number of well-defined proteins with reference to molecular framework, conformational patterns and related structural factors and influences.

Dr. Edsall considered the ques-

tion of whether amino acid residue sequences in peptide chains may be the decisive factor in determining favored three-dimensional configuration of protein molecules.

A graduate of Harvard University, Dr. Edsall received his M.D. degree from Harvard Medical School in 1928. He was awarded Guggenheim Fellowships in 1940 and 1954 and has been Visiting Fulbright Lecturer at Cambridge, England, and Visiting Professor at the College de France, in Paris.

Dr. Edsall is a member or Fellow of numerous scientific societies and former Chairman of the Board of the Federation of American Societies for Experimental Biology. He has served on the editorial board of the *Journal of the American Chemical Society* since 1948 and has been a co-editor of *Advances in Protein Chemistry* since 1944.

The NIH Lectures were established in 1953 to recognize outstanding scientific accomplishments and to contribute to the vital interchange of scientific information.

Patients, Staff, Guests to Participate In CC's Bi-Weekly Reading Night

A bi-weekly Reading Night for CC staff, patients, and visitors was inaugurated last week by the CC Patients' Library and members of the USPHS Officers' Wives Club.

At the first session, on January 25, Dr. Leroy Alldredge, a geophysicist with the Coast and Geodetic Survey, discussed "The Wonderful World of Books."

Reading Nights will be held on alternate Wednesdays in the 14th floor assembly hall of the CC from 7 to 8 p.m. throughout the winter and spring. The next session is scheduled for February 8.

Organized in response to widespread interest, the discussions will

cover books, reading, authors, and libraries. Planned topics include "What Does a Book Offer?," "Our Reading Heritage," "What Good Are Poems?," and "Biographies Bring New Companions."

The audience is encouraged to ask questions, exchange views with the speakers, and participate in general discussion.

Future speakers will include members of the NIH staff and the Bethesda community.

The committee from the USPHS Officers' Wives Club assisting the library staff includes Mrs. William Jenkins, chairman; Mrs. G. Halsey Hunt, Mrs. Frank French, and Mrs. Wilton Fisher.

DR. KETY

(Continued from Page 1)

vestigations in the circulation and metabolism of the brain.

Dr. Kety previously served as Professor of Clinical Physiology and as Assistant Professor of Pharmacology at the University of Pennsylvania Graduate School of Medicine.

Born in Philadelphia, he received his M.D. degree from the University of Pennsylvania in 1940. In 1942 he received a National Research Council Fellowship at Harvard University.

The author of over 100 scientific papers, Dr. Kety is also the recipi-

ent of many honors. Among them are the Distinguished Service Award of DHEW, the Theobald Smith Award, and the Max Weinstein Award.

He is editor-in-chief of the *Journal of Psychiatric Research* and Associate Editor of *Experimental Biology*, and serves on numerous scientific boards, councils, and committees.

Dr. Kety was one of the first NIH scientists chosen unanimously by the Scientific Directors of the Institutes to deliver an NIH lecture, in 1960.

In his new post, Dr. Kety will succeed Dr. John C. Whitehorn, who retired in June 1960.

Science Section

NHI Studies Clarify Role of ADH In Renal Concentrating Mechanism

Studies by Dr. John R. Jaenike, of the National Heart Institute Laboratory of Kidney and Electrolyte Metabolism, have provided evidence to confirm the previously suspected role of antidiuretic hormone in the renal concentration mechanism.

His data indicate that this hormone contributes to the production of a concentrated urine by increasing the permeability of the kidney collecting ducts to water and urea. His findings have been accepted for publication in the *Journal of Clinical Investigation*.

One of the most striking and important features of the mammalian kidney is its ability to put out urine considerably more concentrated than blood plasma when fluid intake is low, and considerably more dilute than plasma when fluid intake is high. By this means the kidney is able to maintain fluid balance so that the organism neither becomes waterlogged nor dehydrated even though fluid intake might fluctuate widely. The hormone which regulates this mechanism is antidiuretic hormone (ADH).

Pituitary Stimulated

When fluid loss exceeds fluid intake, the blood tends to become more concentrated, which increases its osmotic pressure. Special receptors in the brain respond to these increases in osmotic pressures by stimulating the pituitary to release ADH. This hormone promotes water conservation by causing water reabsorption in two adjacent segments of the kidney tubule that in the absence of ADH are impermeable to water: the distal convoluted tubule and the collection duct, which together make up the latter half of the renal tubule.

Blood entering the kidney must flow through filtration structures (glomeruli) where protein-free plasma is removed for processing in the kidney tubules. As the filtrate flows through the first half of the tubule, substances needed by the body are reabsorbed and the volume of the filtrate is reduced some 80 percent by the removal of water. Water removal is the passive result of the active removal of salt, which exerts an osmotic force that pulls the water out behind it.

The reduction in filtrate volume is not accompanied by an increase in filtrate concentration. In fact, since proportionally more solute than water is removed, the filtrate is actually more dilute than plas-

ma when it enters the distal convoluted tubule.

In the distal convoluted tubule and the adjacent collecting duct ADH, by its presence or absence, determines whether the urine will be concentrated or dilute, and its volume relatively small or large. If ADH is absent, neither segment is permeable to water. But salt removal continues in the distal convoluted tubule, and, since water is not removed in proportion, the filtrate concentration drops considerably below that of plasma before the filtrate enters the collecting duct. Urine concentration in the collecting duct is dependent on water removal; and since this segment is also impermeable to water without ADH, the dilute filtrate that entered the collecting duct leaves it as a dilute urine.

If ADH is present, water reabsorption continues in the distal convoluted tubule; and the filtrate concentration may rise as high as that of plasma (but never higher) before it enters the collecting duct, where urine concentration occurs.

Dr. Jaenike found that ADH also increases the reabsorption of water and urea in the collecting duct. His studies revealed that urea concentrations were consistently higher in the medulla and papilla of dog kidneys removed after giving the animals ADH than in those removed after the animals' secretion of ADH had been blocked.

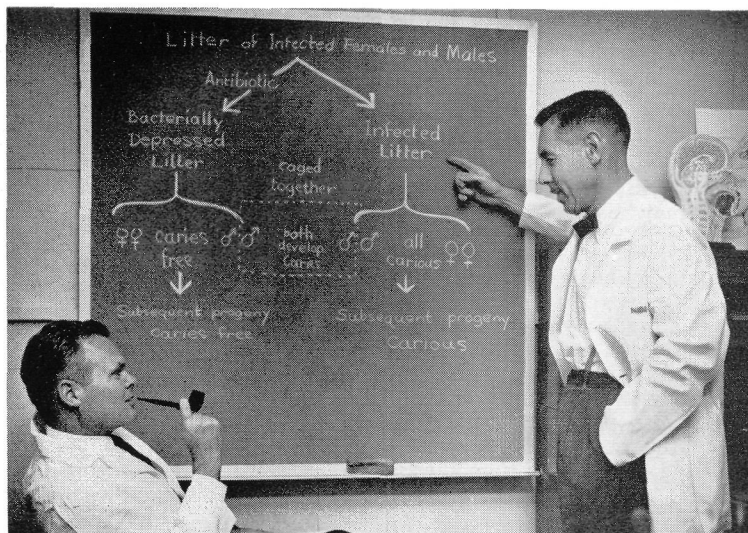
Water Permeability Increased

Because urea reabsorption is dependent upon water reabsorption, the increased reabsorption of urea in these kidney regions where the collecting ducts are located indicated that ADH had increased the water permeability of the collecting ducts. Urine concentration is achieved in the collecting duct by the removal of water; thus this action of ADH is an important factor in the urine concentration mechanism.

The reabsorption of water and urea that occurs in the collecting duct is not due primarily to continued reabsorption of salt, but to the high salt concentrations already existing outside the collect-

(See ADH ROLE, Page 6)

CARIES TRANSMISSION DISCUSSED



Drs. Paul Keyes (right) and Robert Fitzgerald, NIDR scientists, discuss the transmission of the caries-producing flora in hamsters. Infected animals produce infected offspring. The infection can be arrested or eliminated by feeding antibiotics to mother animals whose subsequent offspring remain caries-free unless exposed to other infected animals.

Safe Method Developed For Plasma Transferral

A safe procedure for separating platelets from red blood cells and plasma, using plastic equipment, has been developed by Dr. Allan Kliman, Division of Biologics Standards, and Drs. Emil J. Freireich, Lawrence Gaydos, and Leslie Schroeder, of National Cancer Institute. The work was reported by Dr. Kliman at the January, 1961, Eastern Section meeting of the American Federation for Clinical Research.

The procedure consists of taking whole blood from a donor, immediately separating out the plasma and platelets for transferral to the patient and returning the red cells to the donor.

The return of the red cells makes it possible to withdraw amounts of plasma as large as 1000 ml. per week for periods up to six weeks from the same donor without any harmful depletion of protein or blood cells. Since only one donor is involved, the risk of hepatitis is lessened.

Although repeated doses of platelets from the same donor were administered to each of six leukemic children, the platelet response remained satisfactory and the treatment was repeatedly effective in controlling hemorrhage.

The data obtained indicated that the donor platelets did not provoke specific immunity in the pa-

Effects of Tranquilizer On Nerve Cells Studied

Dr. H. Weil-Malherbe, National Institute of Mental Health Visiting Scientist, who has been studying the distribution of epinephrine (adrenalin) and norepinephrine in the brain nerve cell, has found that they can be separated into two broad fractions: the first present in the cell sap, the second concentrated in granular matter. According to current concepts, the fraction of the cell sap is biologically active; the other is thought to serve as a reserve supply. The effects of the tranquilizer reserpine and a number of other drugs have been examined alone, and in combination with each other.

Findings reported in the *Journal of Neurochemistry* indicate that reserpine acts by effecting a redistribution of amines in the two fractions, and suggest a reappraisal of previous theories on the mode of action of this drug. The results further strongly substantiate other recent research by NIMH investigators indicating the role of catechol-O-methyl-transferase in metabolizing these biogenic amines formed within the brain.

tient studies, and suggests that platelet plasmapheresis may be a practical means of providing therapeutic quantities of hemostatic plasma for thrombocytopenic patients.

Vitamin C Protein Metabolism Role Demonstrated by NIAMD Scientists

Exploration of some of the many biochemical ways in which vitamins can act has disclosed an unusual role for vitamin C (ascorbic acid) under certain experimental conditions. Drs. Bert N. LaDu and Vincent Zannoni of the National Institute of Arthritis and Metabolic Diseases have shown that vitamin C acts to "protect" one of the enzymes needed in the metabolic degradation of tyrosine in the body.

While this protective role is necessary for normal metabolism, it is a much less specific function for vitamin C than had been supposed, and provides an interesting example of the multiple functions the vitamin may have.

Role Important

Vitamin C has been known to have an important role in maintaining normal tyrosine metabolism, a process which takes place in a series of reactions. Before they will take place, however, several enzymes must be present to promote the reactions and control their speed, and at one time it was thought that vitamin C formed part of one of the enzymes, p-hydroxyphenylpyruvic acid oxidase or PPAO.

This enzyme facilitates the second step in tyrosine metabolism,

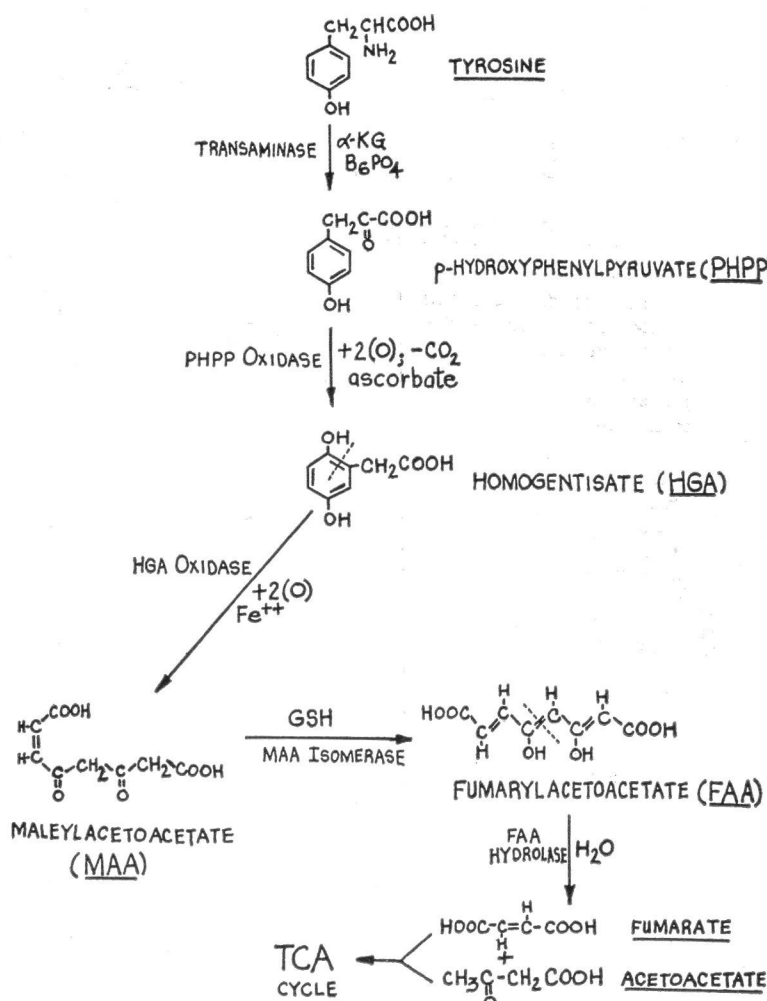
the conversion of p-hydroxyphenylpyruvic acid to homogentisic acid. Such an action by vitamin C would be similar to that of some of the B vitamins which participate in other metabolic processes as indispensable components of the enzymes involved.

The NIAMD scientists have now found that instead of becoming an intrinsic part of PPAO, vitamin C protects this enzyme from being inhibited in the presence of excessive amounts of p-hydroxyphenylpyruvic acid.

Effect Demonstrated

They were able to demonstrate this protective effect in guinea pigs that were deficient in vitamin C and had been fed extra amounts of tyrosine in their diet. The extra tyrosine caused large amounts of

PATHWAY OF TYROSINE METABOLISM IN LIVER



ACTIVATION OF L-TYROSINE OXIDATION

	Rienits	Painter & Zilva	Knox & Knox	Sealock et al.	LaDu & Greenberg
Ascorbic acid	+	+	+	+	+
Isoascorbic acid	—	—	+	+	+
Glucosascorbic acid	—	+	+	+	+
Dichlorophenolindophenol					+
Hydroquinone					+
Reductone				+	
Dihydroxymaleic acid			—	—	—
Glutathione			—	—	—
Cysteine			—	—	—
H ₂ O ₂			—	—	—
Catechol					—
DOPA					—
2-Methyl ascorbic acid				—	
2,3-Dimethyl ascorbic acid				—	
Pteroylglutamic acid	+		—		

Summary of the types of compounds tested for ability to replace ascorbic acid in the oxidation of L-tyrosine by cell-free liver preparations. +, effective; —, ineffective; blank, not tested. (Ref. 69, 63, 39, 80, 42).

p-hydroxyphenylpyruvic acid to accumulate in the liver and within two hours 80 percent of the PPAO present in the liver had been inactivated.

On the other hand, animals that were given vitamin C showed no reduction in PPAO activity after tyrosine loading, indicating that the vitamin prevented inactivation. The exact mechanism of this inactivation and protection is still being investigated.

Other Compounds Used

Other compounds chemically unrelated to vitamin C, including the blue dye 2, 6-dichlorophenolindophenol, were also able to prevent inhibition of the enzyme in ascorbic acid-deficient guinea pigs given large amounts of tyrosine.

However, these compounds did not prevent guinea pigs from developing weight loss, hemorrhages and other signs of scurvy (vitamin C deficiency).

Conclusions Cited

"Perhaps future experiments will reveal instances in which ascorbic acid acts as a 'conventional' vitamin in some of the other biochemical processes which are deranged in scurvy. The elucidation of its role in tyrosine metabolism illustrates one of the variety of ways in which this essential carbohydrate participates in biochemical and physiological reactions," the NIAMD investigators concluded.

The work was reported at the New York Academy of Sciences "Conference on Vitamin C."

EFFECT OF FEEDING TYROSINE ON ENZYMES IN NORMAL AND SCORBUTIC GUINEA PIGS

Enzymes	Normal		Scorbutic	
	Untreated(6)	Treated(6)	Untreated(10)	Treated(10)
μM substrate oxidized/hr./gm. tissue				
Liver				
Tyrosine Transaminase	18	24	40	87
PHPP Oxidase	30	25	17	3
HGA Oxidase	127	133	70	101
Kidney				
PHPP Oxidase	7	5	7	1

PREVENTION OF P-HYDROXYPHENYLPIRUVIC ACID OXIDASE INHIBITION IN VIVO BY VARIOUS COMPOUNDS

Compound*	Liver P-HPP Oxidase μM/hr./gm.	Plasma Levels		Liver "Ascorbic Acid" mg. %
		L-Tyrosine mg. %	P-HPP mg. %	
None (6)	1.6	50.3	5.6	3.1
L-Ascorbic (4)	32.2	12.5	< 0.4	28.9
D-Isoascorbic (4)	31.0	13.2	< 0.1	13.3
D-Glucoascorbic (4)	9.5	24.5	0.8	4.5
2,6-DCPP, ox. (5)	29.0	10.2	< 0.1	2.6
2,6-DCPP, red. (4)	29.5	5.9	< 0.1	3.3

*10 mg. injected I.P. 30 minutes before first tyrosine feeding and 10 mg. again 2 hours later.

Intratracheal Inoculation With Polyoma Virus Studied in Hamsters

The increasing prevalence of human carcinoma of the lung has highlighted the urgent need for studying the disease in the laboratory. A most important step is the production of lung tumors in the laboratory animals, and a number of reports have appeared in the scientific literature on the methods—particularly by the use of hydrocarbons—that will induce such tumors in mice, rats, and rabbits.

Syrian Hamsters Used

The Syrian hamster appears to be a suitable animal for the study of lung carcinogenesis, because spontaneous lung tumors have not been observed in this species and pulmonary infections are rare.

About two years ago, Drs. Bernice Eddy (Division of Biologics Standards) and Sarah E. Stewart (National Cancer Institute) reported that subcutaneous inoculation of polyoma virus induced undifferentiated lung tumors in newborn hamsters. This observation provided an opportunity to investigate the possible viral etiology of lung cancer, and was the basis for the present study by Dr. Alan Rabson and his associates of the effect of intratracheal inoculation of the virus in hamsters.

Tumors Developed

Of 22 weanling (26-38 days old) animals inoculated, 16 died by the 400th day. Lung tumors with histologic features of bronchiolar carcinoma, alveolar-cell carcinoma, and squamous-cell carcinoma were found in six hamsters that died 164 to 391 days after inoculation. Of the 10 animals in which no tumors were seen, five that died 27 to 195 days after inoculation were found to have proliferation lesions of bronchiolar and alveolar-lining cells. One of the tumors has been transplanted, and has retained its squamous differentiation through four generations.

An attempt was made to demonstrate the presence of free virus by adding a suspension of one of the lung tumors to tissue cultures of milk-adapted P388 D₁ cells. However, no evidence of a cytopathic effect was observed.

Further work is in progress to investigate the role of the polyoma virus in the production of these tumors.

The report, which appears in a recent issue of the *Journal of the National Cancer Institute*, was written by Dr. Rabson, of the NCI's Pathologic Anatomy Branch, and William J. Branigan and Frances Y. Legallais, of the Laboratory of Pathology.

Acetylcholine Production Discussed

Dr. David Nachmansohn, Professor of Biochemistry at the Columbia University Medical School, delivered a National Heart Institute-sponsored lecture entitled "The Chemical Basis of Nerve Activity" on January 12 in the 14th floor auditorium of the Clinical Center.

Recent investigations conducted by Dr. Nachmansohn and his colleagues into the fundamental mechanisms of nerve conduction have confirmed his theories, first proposed in 1940, concerning the vital role of acetylcholine in all bioelectrical functions.

The studies show that acetylcholine production progresses along the entire nerve fiber where it combines with a receptor protein to change the nerve's permeability to ion movements. This change progressively alters the nerve's electrical potential, allowing propagation of the nerve impulse. The duration of the impulse is controlled by cholinesterase, which destroys the acetylcholine a fraction of a second after it acts.

Prior to these studies, most scientists believed that acetylcholine production occurred only at nerve endings and that it was respon-

sible for conducting impulses across the endings to other nerves and muscles. Their belief was based on studies of the action of curare, an impulse-blocking poison which apparently acted only at nerve endings.

Myelin Sheath Studied

Dr. Nachmansohn, however, theorized that curare would act at any point along the nerve were it not for the fatty insulating layers (myelin sheaths) surrounding nerves. This was demonstrated in studies involving the physical or enzymatic destruction of myelin sheaths.

The Columbia University workers also isolated and identified the receptor protein with which acetylcholine combines to change membrane permeability, and found that local anesthetics combine specifically with the protein in a water solution. They believe that this is the first conclusive demonstration of the specific chemical reaction by which local anesthetics produce their effects.

Sodium Phytate Found To Be Caries Inhibitor

Addition of soluble mineral phosphates to the diets of laboratory animals has consistently demonstrated the cariostatic effect of this group of compounds. Although the exact mode of action is obscure, National Institute of Dental Research scientists have felt that an inhibitory reaction may be occurring locally on the surfaces of teeth in the presence of freely available phosphate ions.

Recent studies with sodium phytate, an organic phosphate, have now demonstrated a cariostatic effect of possible systemic origin. Dr. F. J. McClure, Chief, Laboratory of Biochemistry, NIDR, has found that an otherwise cariogenic diet containing 1.4% sodium phytate, when fed to rats, reduced the caries incidence in these animals by an average of 77%.

This anticaries effect was significant when compared with a 51% reduction obtained with sodium phosphate and a 72% reduction with diammonium phosphate, both administered at comparable levels in similar diets. The substantial caries reduction was somewhat unexpected since phytate is hydrolyzed primarily in the lower intestine by the enzyme phytase. In addition, data from serum analysis of blood from animals receiving sodium phytate confirmed the systemic availability of phosphorus in these animals.

The caries inhibiting effect of

NCI Leukemia Studies Show Changes in Level Of Serum Protein

Certain characteristic changes in serum protein levels that appear in patients with two types of acute leukemia have been reported by scientists of the General Medicine Branch, National Cancer Institute.

This investigation of serum protein patterns in leukemia is part of the continuing NCI study of metabolic changes in malignancy.

The study included 110 patients who were admitted to the Clinical Center of the National Institutes of Health over a 5-year period. The levels of five protein components in the serum were measured by electrophoretic analysis of 171 samples from 82 patients with acute lymphoblastic leukemia (LL) and 64 samples from 28 patients with acute myeloblastic leukemia (ML).

Characteristic serum protein patterns were observed for the two types of acute leukemia. In ML, the gamma globulin level was elevated; in LL, the alpha-2 globulin level was elevated. In both forms of the disease, serum albumin was significantly lowered and the beta globulin component was essentially normal. Alpha-1 and alpha-2 globulin levels both exhibited a wide range of values.

These abnormal serum protein patterns were characteristic of the uncomplicated disease, i. e., excluding samples obtained during fever, infection, or liver disease. Fever, in the absence of infection, was associated with elevation of the alpha-1 globulin component in both types of the disease. Bacterial infection was also associated with elevation of this component, and, in addition, with a further decrease in the serum albumin levels.

The characteristic serum patterns persisted during hematologic remission and following therapy with antimetabolites or adrenal corticosteroids.

The authors of the paper conclude that the "serum protein alterations . . . appear to be specifically due to the presence of the leukemic processes. . ."

The study is reported in a recent issue of *Blood* by Drs. John L. Fahey and Dane R. Boggs.

organic phytate remains speculative, particularly when viewed in light of the proposed local action of the several mineral phosphates. However, data from these studies lend further support to observations of other investigators that the organic phosphates (primarily phytate) present in unrefined carbohydrate foods, are responsible for the low cariogenic activity of these foods.

Radium Holder DeVised For Use in Nasopharynx

Effective treatment of certain tumors of the nasopharynx may require the use of an internal source of radiation—in the form of radioactive isotopes—to supplement an external source. A number of devices have been employed as holders for the isotopes.

A simple method of preparing an accurate plastic mold of the nasopharynx for this purpose has now been reported by scientists of the National Cancer Institute's Radiation Branch and a colleague of the Dental Department of the Clinical Center.

The method consists of forcing dental compound into the nasopharynx to form an impression, which is hardened quickly by cooling and duplicated in a mold of acrylic resin plastic. The radiation source is inserted into the mold, which is then positioned in the nasopharynx.

The procedure takes 60 to 75 minutes, during which the patient remains under anesthesia. For most tumors, no surgery is required.

A mold containing radium was used at the Clinical Center to deliver a total of 3,000 roentgens in two exposures ten days apart to a rhabdomyosarcoma in a five-year-old girl. Only 400 roentgens

(See RADIUM HOLDER, Page 6)

Futher Studies Made On Leukemia L1210

Further results of a continuing study of the interrelationships of host-tumor-drug factors in the L1210 mouse leukemia have been reported by investigators of the National Cancer Institute's Laboratory of Chemical Pharmacology.

Their earlier studies had indicated that mice surviving systemic leukemia L1210 following treatment with drugs showed immunity to reinoculation of drug-sensitive and drug-resistant sublines of the leukemia. This finding suggested the possibility of utilizing the immune response to enhance the effectiveness of chemotherapy of mice bearing variant forms of the disease resistant to specific drugs or classes of drugs.

Mice Inoculated

Mice were inoculated on day 0 with a subline L1210Z, which is sensitive to therapy with antifolic drugs, and on day 7 with a subline, M46R, which is resistant to antifolic drugs.

Treatment with 3', 5'-dichloroamethopterin (DCM), started on day 7, when the sensitive disease had become systemic, produced a median survival time of approximately 40 days from the day of inoculation of the resistant subline.

On the other hand, the survival time of DCM-treated mice bearing only the resistant subline did not exceed 20 days, even if treatment was started on the day of implantation. Furthermore, if the mice were inoculated with both lines and treatment was started on the same day, they survived no longer than treated mice bearing only the resistant subline.

Survival Prolonged

The findings show that it is possible to prolong the survival of mice bearing an antifolic-resistant variant of leukemia L1210 and receiving treatment with DCM by prior inoculation with a drug-sensitive subline.

It appears that the presence of systemic sensitive leukemia L1210 elicited in the hosts an immune response, which contributed to the therapeutic effect of DCM against the resistant variant. Further study of the relationship of drugs to immunological inhibition and enhancement continues to seek a basis for improved cancer therapy.

Dr. Abraham Goldin, Stewart R. Humphreys, Gerald O. Chapman (now with the Cancer Chemotherapy National Service Center), John M. Venditti, and Dr. Michael A. Chirigos are co-authors of the report, which appears in a recent issue of *Cancer Research*.

NHI Devises More Precise Clinical Test For Hyperparathyroidism Diagnosis

Scientists of the National Heart Institute Clinical Endocrinology Section have devised a new clinical test for hyperparathyroidism that affords a more precise diagnosis of this disorder than do tests used previously.

The new test involves feeding a diet low in calcium and phosphorus over a period of 13 days and giving aluminum hydroxide orally during the last 10 days of the regimen. The diagnosis of hyperparathyroidism is established if the subject's urinary calcium exceeds 250 mg. per day during the test period.

The diagnostic criteria normally used to establish hyperparathyroidism are excessive serum calcium, excessive urinary calcium, and abnormally low serum phosphorus.

However, all of these criteria are not met in many cases of hyperparathyroidism; and some of them, notably hypercalcemia, may be due to other causes. Thus, this disorder often presents a ticklish problem of differential diagnosis.

New Test Evaluated

The new test appears to overcome many of these problems. It was evaluated in 10 normal controls and in 18 patients with established hyperparathyroidism, but only four of which met all of the diagnostic criteria above. When put on the test regimen, however, all 18 patients exhibited abnormally high urinary outputs of calcium—defined as a rise in urinary calcium above 250 mg. per day regardless of values of serum calcium or of serum and urinary phosphorus. In contrast, the urinary calcium of the normal controls never exceeded 230 mg. per day.

RADIUM HOLDER

(Continued from Page 5)

reached the tumor-free area of the nasopharynx and the nearest portion of the midbrain.

The investigators conclude that the method is advantageous because the mold is easy to make and the accurate outline of the tumor guides the positioning of the radiation source.

The report appears in a recent issue of the *American Journal of Roentgenology*. The coauthors are Drs. Herman D. Suit (now with the M. D. Anderson Hospital, Houston, Texas), J. Robert Andrews, and Stanley S. Sneider (now with the Jackson Memorial Hospital, Miami, Florida) all of the National Cancer Institute, and Dr. Ralph S. Lloyd, of the Clinical Center.

The specificity of the new test was further verified by the observation that urinary calcium reverted to normal in five patients tested after surgical correction of their hyperparathyroidism, whereas it became abnormal in controls tested after they had been given parathyroid hormone.

Test More Accurate

The aluminum hydroxide administered as part of the test effectively converts a low phosphorus intake into a very low one by interfering with the absorption of phosphorus from the intestine. It also appears to enhance calcium absorption in hyperparathyroid subjects to a much greater extent than in normal subjects. This action of the aluminum hydroxide, though not completely understood, appears to be chiefly responsible for the specificity of the test.

The new test, especially when used in combination with the calcium infusion test previously found to be a reliable means of diagnosis, allows diagnosis of hyperparathyroidism with greater accuracy and precision than heretofore possible, and is especially valuable in the difficult-to-diagnose case.

The new test was devised by Drs. Pacita Pronove, Norman H. Bell, and Frederic C. Bartter, of the NHI Laboratory of General Medicine and Experimental Therapeutics. Their findings were reported at the recent meeting of the American Federation for Clinical Research in New Orleans.

ADH ROLE

(Continued from Page 3)

ing duct. The potent osmotic force exerted by the salt, which pulled the water out, cancels out the osmotic force exerted by the concentrated waste products inside the collecting duct which tends to pull the water back into the tubule.

The reabsorbed urea contributes to maximum urine concentration by balancing off the urea still remaining inside.

Since about 80 percent of the water entering the tubules has already been reabsorbed before ADH enters the picture, it might appear that the contribution of this hormone to water conservation is slight. However, since the kidney processes a volume of fluid equal to about four times the total body water every 24 hours, relatively small losses quickly add up to staggering totals. Such fluid losses, due to inadequate ADH, are responsible for the insatiable thirst and enormous urine output that attend diabetes insipidus.

Garter Snake Indicated As Possible WEE Host During Winter Months

The method by which the virus of Western Equine Encephalitis maintains itself during the winter months has long puzzled epidemiologists engaged in the study of this disease. Although it is established that birds play a part in its dissemination during the summer, their role as a winter reservoir host or as a means of reintroducing the virus into northern areas each year needs further clarification.

Snakes Tested

The observation by Drs. Leo A. Thomas and Carl M. Eklund of the National Institute of Allergy and Infectious Diseases' Rocky Mountain Laboratory that *Culex tarsalis* overwinters in rockpiles along with hibernating garter snakes, led to speculation on the possibility of a snake reservoir. Preliminary tests demonstrated the susceptibility of the reptile to WEE virus infection with a resulting viremia of high titer and long duration.

The present study further clarifies the problem and indicts garter snakes as one possible overwintering mechanism for the WEE virus. Findings were reported in the *Proceedings of the Society for Experimental Biology and Medicine*.

Virus Detected

In the experiment, the investigators inoculated 50 wild garter snakes intraperitoneally with virus-infected mouse brain suspension in September and November of 1959. The snakes were then placed inside a specially constructed cage and allowed to hibernate under simulated natural conditions.

During March, April, May and June the snakes reappeared and after a short period, virus was detected in their blood in high titer for periods up to 70 days following emergence.

The scientists identified virus in 16 inoculated snakes and complete virus transmission from snakes through mosquito to chick was shown in four. For transmission, uninfected *C. tarsalis* mosquitoes were fed on the post-hibernating snakes with viremia and held from 9 to 23 days before being allowed to feed on a non-infected 1-day-old chick. In the four cases of demonstrated transmission, virus was isolated from the mosquitoes fed.

Although the data demonstrate a possible overwintering mechanism of WEE virus, Dr. Thomas notes that more conclusive evidence will be available if virus is isolated from garter snakes actually collected in the field.

CONFERENCE

(Continued from Page 1)

early establishment of a National Institute of Gerontology within the framework of the National Institutes of Health.

Two Congressmen reported that they are sponsoring plans for organizations to deal with the special problems of the aging.

Sen. Patrick McNamara of Michigan explained his proposal for an Office of Aging within DHEW, and Rep. John E. Fogarty of Rhode Island described his bill for a Federal Commission on Aging, which he introduced in the House on January 9.

Rep. Fogarty introduced the original bill (H. R. 9822) which as Public Law 85-908 authorized the President to call the Conference, designating the Secretary of HEW to plan and conduct it with the assistance of Federal departments and agencies.

3,200 Attend

The delegates and visitors from 26 foreign countries, totaling 3,200, divided into 20 sections, each with its chairman, technical director, and recorder.

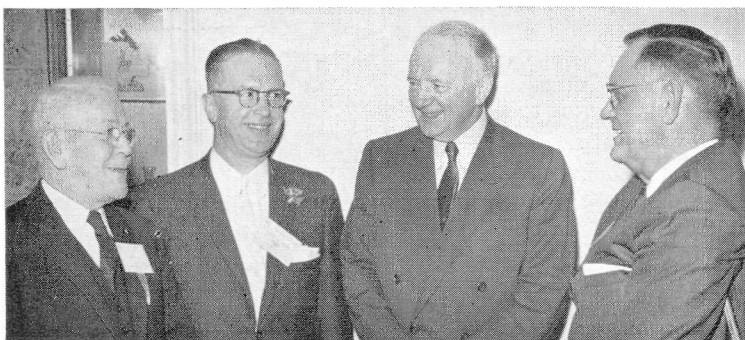
These met in work groups or sections and addressed themselves to their subjects: Population Trends, Income Maintenance, Impact of Inflation on Retired Citizens, Employment Security and Retirement, Health and Medical Care, Rehabilitation, Social Services, Housing, Education, Role and Training of Professional Personnel, Family Life, Free Time Activities, Religion and Aging, Research in Gerontology (Biological, Medical, and Psychological and Social Science), Local Community Organization, State Organizations, National Voluntary Services and Service Organizations, and Federal Organizations and Programs.

Folsom Endorses Plan

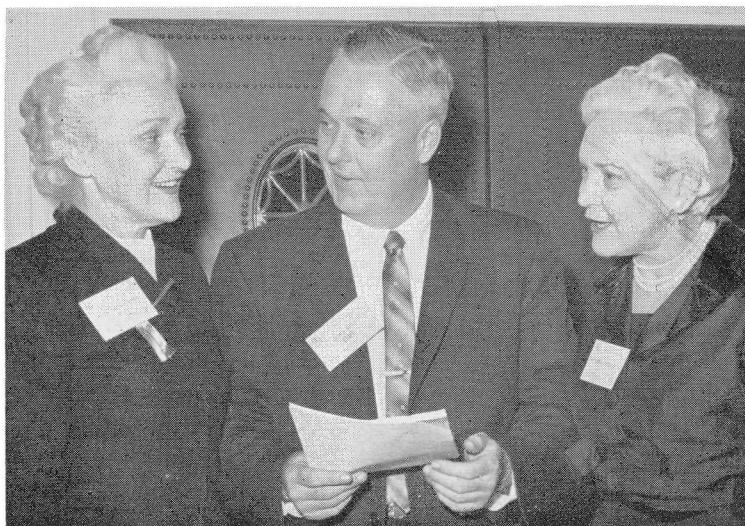
Former Secretary of HEW Marion Folsom endorsed the Social Security plan for medical care, with the proviso that an advisory council representing employers, labor, the insurance industry, hospital administrators, the medical profession, and the general public be appointed to study all aspects of the problem and make recommendations to Congress.

The final policy statements of the Conference groups included a recommendation that "... a Federal coordinating agency in the field of aging be given: a) a statutory basis and more independent leadership, b) adequate funds for coordination and other assigned functions through a 'line item' appropriation, c) responsibility for formulation of legislative proposals for submittal to Congress, and d) responsibility for periodic reviews of reports on the various

OFFICIALS MEET AT CONFERENCE



Robert H. Grant, Executive Officer, NHI, and Director of the Special Staff on Aging (second from left), during a Conference interlude chats with John E. Raine, Chairman, Virginia Commission on Aging (left); U. S. Sen. Harry Flood Byrd (second from right), and H. Burton Aycock, HEW Regional Representative for Aging, Region 3, Charlottesville, Va.



Dr. James Watt, NHI Director and Special Assistant to the Secretary for Aging, confers with Margaret Schweinhaut, Chairman, Governor's Commission on Aging, Maryland (left), and her twin sister, Marie McGuire, who attended the Conference as a delegate from Texas.—Photos by Jerry Hecht.

Federal programs, Departments and agencies working in behalf of older people, to achieve their effective coordination and operation."

The Conference Research Sections recommended that DHEW, through PHS and NIH, continue to foster its program of supporting large-scale interdisciplinary research centers in aging.

They pointed out the advantages of simultaneously bringing together the efforts of many disciplines with resulting intellectual cross-fertilization and program stability, the attraction of young investigators to the program, and, as a final product, new information of importance.

The Sections reported that these programs are having "an immense impact on the field of aging with each center serving as a regional resource for community assistance in the health-related aspects of aging."

Summing up highlights of the

A Guard Office Reminder: Check It for Lost Articles

The Guard Office, Bldg. 10, Rm. 1-A-106, usually has a collection of jewelry, keys, gloves, coats, etc. which have been found somewhere on the reservation. Remember to check there when you or your visitors lose things.

Conference, former HEW Secretary Flemming observed, "The Conference demonstrated America at its best." He expressed deep appreciation for the "quality of participation," adding, "Medical care is one of the major issues confronting our Nation today. I am convinced that the issue cannot be resolved by relying solely on private efforts. The Federal Government must become a partner."

Dr. Haas Retires After 30 Years In Health Service

Dr. Victor H. Haas, who was the first Director of the National Institute of Allergy and Infectious Diseases, retired January 1 from the Public Health Service after 30 years of service. Dr. Haas had been associated with NIH since the early 1930s, his first assignment here dating back to 1934.

In the course of his career he worked on encephalitis investigations in St. Louis, on plague in San Francisco, and in the late 1930s on viruses in Bethesda.



Dr. Haas

In 1941 Dr. Haas was sent with a group of Public Health Service officers to head the Medical Commission to the Yunnan-Burma Railway in China.

Wins Legion of Merit

In 1942-1943 he was attached to a U. S. Army unit of the China-Burma-India Theater after work on the railroad was made impossible by early reverses during the war. For his service during this period he was awarded the U. S. Army Legion of Merit.

From 1943-1948 Dr. Haas served as Officer-in-Charge of malaria investigation, and in 1948 he became the first Director of NIAID, then named the National Microbiological Institute.

In April of 1957 he left the directorship of the Institute for full-time research in the Laboratory of Infectious Diseases.

In 1959 a reorganization of the laboratory structure of NIAID resulted in the formation of several new laboratories, one being the Laboratory of Biology of Viruses, to which Dr. Haas remained attached until his retirement.

For the past 13 years Dr. and Mrs. Haas lived in Bethesda. They have now left the area and expect to settle near San Francisco.

Meenehan to Address NIH Camera Club

John Meenehan, well-known Washington lecturer on color photography, will be guest speaker at the next meeting of the NIH Camera Club, to be held in Wilson Hall, February 6, at 8 p.m.

As color photography chairman for the Greater Washington Council of Camera Clubs Inter-club competitions, he will discuss the techniques of preparing potentially prize-winning color slides.

Registration Dates Set For Graduate Courses

Registration for the spring term of the USDA Graduate School will be held here February 6-11 from 11:30 a.m. to 4:30 p.m. daily, in Room 2-B-50, Clinical Center.

Catalogues are available from all administrative and personnel offices, the library, and the CC reception desk.

The following changes in the courses given at NIH have been made since the catalogue was issued:

On Monday, Special Pathology and Chemical Quantum Mechanics are omitted. A new course in Ordinary Differential Equations will be taught by Dr. Clifford S. Patlak.

On Tuesday, the course in Microbial Biochemistry has been dropped, and will be given instead on Wednesday night by Dr. William B. Jakoby.

On Wednesday, the instructor for Introduction to Determinants and Matrices has been changed to Dr. Clifford S. Patlak. A new course in Introductory Virology will be taught by Dr. Wallace P. Rowe.

The Thursday schedule has not been changed.

For further information call Carol Long, Ext. 2427, Bldg. 10, Rm. 2-B-50.

DR. TERRY

(Continued from Page 1)

defects or of heart damage due to disease;

Clinical evaluation of new drugs for the treatment of hypertension and congestive heart failure; and

Studies on endocrine factors such as adrenal, thyroid, pituitary, and other hormones in cardiovascular disease.

Of special interest to Dr. Terry were the studies on amines, many of which appear to be intimately involved in the mechanisms by which the body regulates its blood pressure.

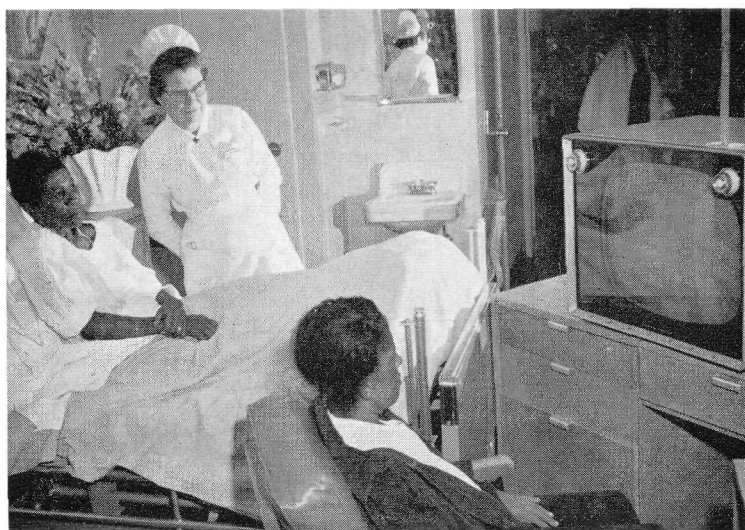
Evidence Is Clear

It has never been shown that amines *per se* are villains in essential hypertension; however, it has become abundantly clear that certain drugs which alter amine metabolism also lower blood pressure in hypertensive patients.

The two amines that have been studied most intensively are norepinephrine and serotonin. These amines not only figure most prominently in the action of many drugs used against hypertension—norepinephrine in their hypotensive action, serotonin in their sedative and tranquilizing effects—but they also play important roles in the syndromes of two types of secreting tumors: malignant carcinoid and pheochromocytoma. Dr. Terry participated directly in some of the

CC PATIENTS WATCH MUSICAL ON TV

Story on Page 1



"Annie Get Your Gun," the Hamsters' musical production, was shown especially for patients on January 17. The NIH closed-circuit TV system brought the show to those unable to attend in the auditorium. Patients Roxie Broadnax (left) and Ann Roundtree watch the show in their room with Nurse Virginia McCormick. The image on the TV screen was obscured by the flash bulb, despite special efforts by Photographers Bob Pumphrey and Sam Silverman.

most important NHI studies on these two amines.

Malignant carcinoid produces a many faceted syndrome whose symptoms include flushes and cyanosis, acute GI and respiratory distress, and heart damage. Dr. Terry and Drs. Albert Sjoerdsma and Sidney Udenfriend were able to confirm that this syndrome was due to the large amounts of serotonin secreted by this tumor.

Studies on the metabolism of serotonin in connection with this work led to the development of a simple urinary test for the diagnosis of malignant carcinoid.

Secretes Norepinephrine

Pheochromocytoma is a tumor that secretes large quantities of norepinephrine, which is responsible for the elevated blood pressure accompanying this disease. Studies on this tumor by the same research team, with Dr. L. C. Leeper, helped to clarify the metabolic pathways by which norepinephrine is produced and broken down by the body.

Dr. Terry also collaborated with Drs. Sjoerdsma, Louis Gillespie, and other NHI scientists in clinical studies on the monoamine oxidase inhibitors—a family of drugs showing great promise in the treatment of hypertension.

These drugs inhibit monoamine oxidase, an enzyme which inactivates a number of amines including norepinephrine and serotonin, and lower blood pressure by a mechanism still incompletely understood.

Unfortunately, the early MAO inhibitors tested proved too toxic for therapeutic use; however, so great was the promise of this

APPOINTMENTS

(Continued from Page 1)

fessor of Medicine and of Preventive Medicine and Public Health. He was at that time assigned to active duty as a Medical Service staff member of the U.S. Marine Hospital in Baltimore (now the U.S. Public Health Service Hospital).

In August 1943 he was appointed Chief of the Medical Service, and in 1950 joined the General Medicine and Experimental Therapeutics Branch of the then recently established Heart Institute. He was named Chief of that Branch in 1951 and continued in that capacity when the Branch was transferred from Baltimore to Bethesda in 1953.

From 1944 to 1953 Dr. Terry was also a part-time Instructor in Medicine at Johns Hopkins University. In the latter year he was named Assistant Professor in Medicine there, and has since continued in that capacity on a part-time basis.

A native of Red Level, Ala., Dr.

earlier work that NHI scientists did not give up on this family, and a new drug now undergoing trial shows every sign of amply rewarding their patience.

After he became Assistant Director of NHI, Dr. Terry, despite the press of administrative duties, followed closely the clinical studies of the Institute, particularly those of his old Branch and the patients who had been under his care during the course of his research studies.

Dr. Sjoerdsma Honored For Metabolic Studies

Dr. Albert Sjoerdsma, Head of the Experimental Therapeutics Branch, NHI, was one of 22 scientists presented gold medallion medical achievement awards by the Golden Slipper Square Club at its "Salute to Medicine" dinner in Philadelphia on January 5.



Dr. Sjoerdsma

The award winners, all distinguished medical scientists, included Drs. Stanhope B. A. Jones, Carl V. Moore, Michael E. DeBakey, John H. Gibbon, Jr., Howard A. Rusk,

Selman A. Waksman, and Paul D. White.

Dr. Sjoerdsma's award was in recognition of his clinical and experimental studies of the metabolism of vasoactive amines. His work in this field has revealed much of what is known about amine-secreting tumors: malignant carcinoid, pheochromocytoma, and mast cell tumors.

Terry attended high school there and was valedictorian of the Class of '27.

He received his B.S. degree from Birmingham-Southern College in 1931, and attended the School of Medicine of Tulane University, where he received his M.D. degree in 1935, ranking fourteenth in a class of 120.

Following World War II, Dr. Terry was a member of the Medical Division of Strategic Bombing Survey to Japan. In 1949 he served as a staff member of the Senate Sub-committee Investigating Malmédy Atrocities.

Directs Training Program

From 1950 to 1955 he was a member of the Cardiovascular Study Section, NIH, and has been a member of the Medical Board of the Clinical Center since 1953, serving as its chairman from 1953 to 1955.

He was Chairman of the Cardiovascular Research Training Committee of the Heart Institute in 1957, and from 1956 to 1958 was a member of the PHS Committee on Civilian Health Requirements.

Since 1953 he has served as Director of the Residency Training Program of the Heart Institute, and since 1957 as a member of the Advisory Committee on Nutrition of the Indian Health Service.

Dr. Terry is married to the former Beryl Janet Reynolds. They have three children: Janet, 17; Luther, L., Jr., 15; and Michael, 14. Their home is at 105 South Van Buren St., Rockville, Md.